14 **TITLE** **PROJECT NO.** [redacted]

[illegible] 13 **BOOK NO.** [redacted]

Investigator(s): H. Brich Date: [redacted]
Notebook/page #: Microsphere lot #: 94381-11

Microsphere Production

Process Room Conditions

Room Temp.:	22°C
Room Humidity:	51.5% RH

Polymer Preparation

Polymer type 1:	PEG-PLGA
Source & Lot no.:	BPI, Lot # 04-14-19
Mass (g):	3.60 g
Polymer type 2:	DL-PLA
Source & Lot no.:	BI Lot # 34038
Mass (g):	3.61 g
Solvent Type:	MeCl₂
Source & Lot no.:	EM, lot no 35068
Volume:	240 mL
Surfactant type:	Lecithin
Surf. (Wt/Vol):	25 mg
Dissolution Method:	Stirring
Dissolution Temp.:	Room temperature
Dissolution Time:	1h15
Excipient 1:	H_2O
Source & Lot no.:	House DI
Amount, wt:	3 mls
Comments:	Dissolve ammonium acetate in water as follows: 108 g in [illegible] of H.D. Add [illegible] to polymer solution.

Aeration Methodology

Sonication:	None
Horn type:	
Frequency:	
Power:	
Temperature:	
Time:	
Time until spray:	
Sparging:	None
Gas type:	
Gas pressure:	
Temperature:	
Time:	
Time until spray:	
Homogenization:	VIRTIS
Blade type:	Macro ultra-fine generator
Time:	1 minute [illegible]
Speed:	20,000 RPM
Temperature:	Ice bath
Time until spray:	~1 minute
Comments:	

Spray Conditions

Cleaning Proc.:	Vacuum production, MeCl₂ thru nozzle
Nozzle type:	0.7mm standard, unit B
Gas Pressure:	45 psi
Gas Flow rate:	600 L/h
Gas type:	N₂ medical grade
Feed Flowrate:	112 rpm
Inlet Temp.:	50°C
Start Time:	1:16
Finish Time:	1:38
Mass Recov'd:	16.3 − 14.71 = 1.47
Yield (%):	17%

Process Conditions	Start 1:17	Middle 1:27	Finish
Outlet Temp.:	24°C	25°C	23°C
Filter Vacuum:	−40 mbar	−[illegible] mbar	−[illegible] mbar

Comments: Did not tape inlet tube as it had been of a previous batch.

Drying Methodology

Type:	Lyophilization VIRTIS Genesis [illegible]
Total dry time:	[illegible]
Mass recovered:	[illegible] 18.485 − 16.[illegible] = 1.73 g
Yield (%):	[illegible] 25%
Comments:	[illegible]

Sizing Methodology

Room Temp.:	
Room Humidity:	
Screening Time:	
Screen sizes:	
Screen type:	
Product recovered:	
Yield (%):	
Comments:	

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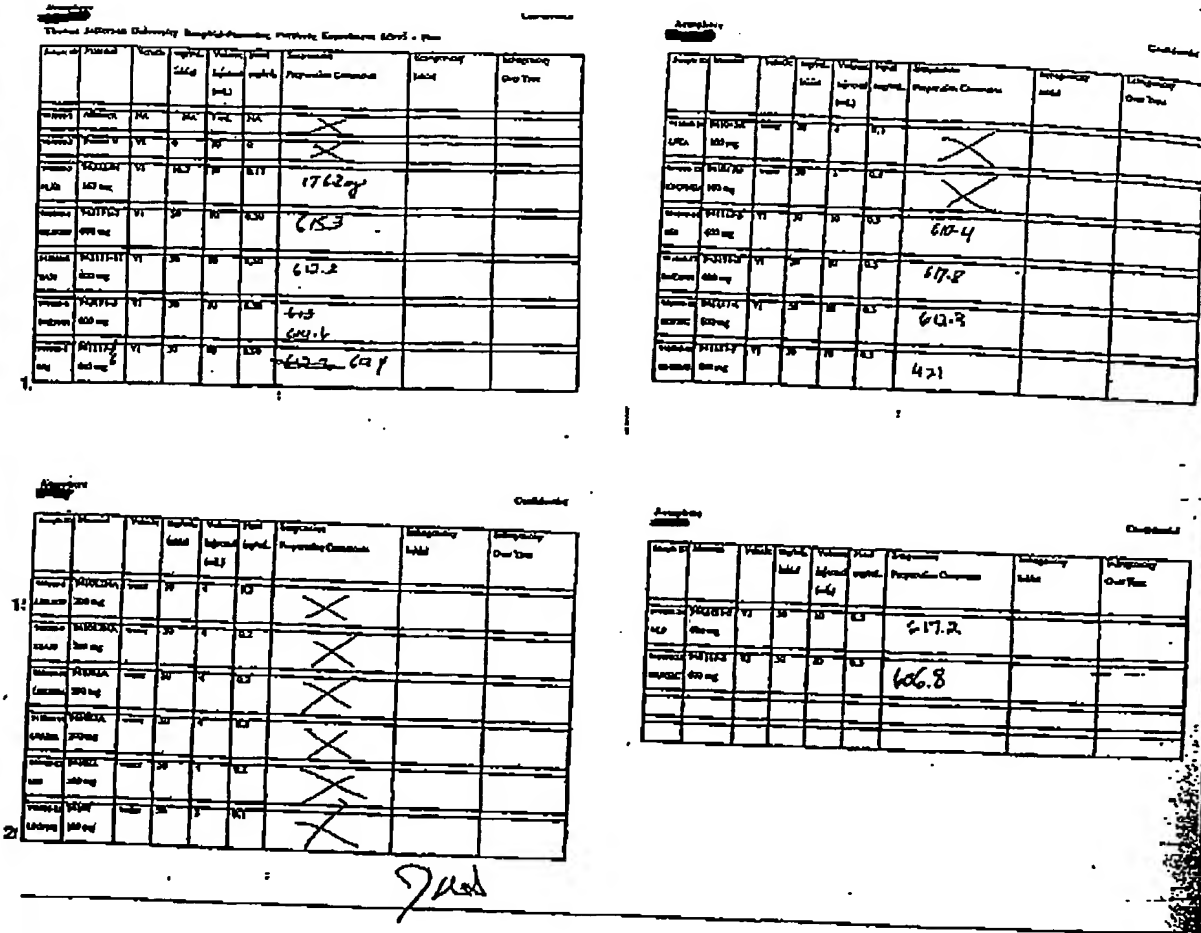
80 TITLE TJU Study For [redacted] PROJECT NO



Samples weighed by Howard in DryBox on [redacted]. All but the 941082 and 941083 samples sent to Fossberg on [redacted] by Ausborn on dryice/gel pak

SCIENTIFIC INVENTIVE PRODUCTIONS CHICAGO [redacted] Made in USA

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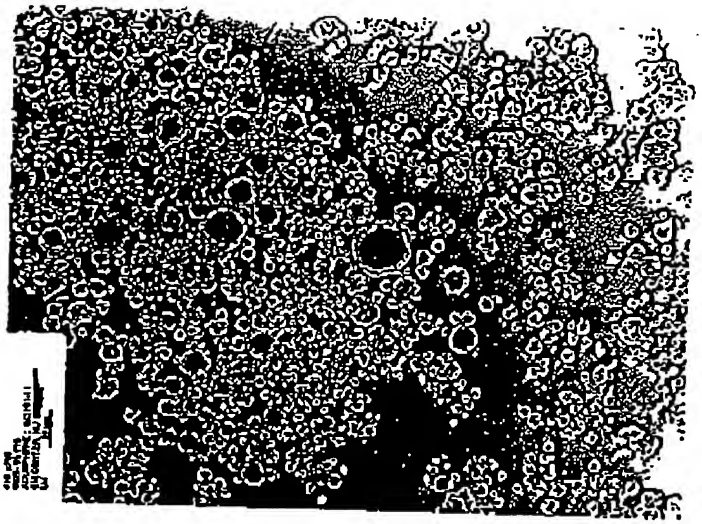

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106 TITLE PROJECT NO

Acceptance
[redacted]

Notes

All samples will be prepared by vortexing and sonication.

All samples will be preweighed in 20 mL scintillation vials. Empty 20 mL scintillation vials will be brought.

Saline (0.9%) will be used instead of water for the bulk fluid in the pumping system. Preweighed samples of 16.2 g of NaCl will be brought over, and mixed to 1800 mL with water in a bottle. Two such bottles will be sent to TJU. A total of 20 NaCl vials will be brought.

Vehicle 1 = 0.9% Tween 20, 3% glycerol ← never used

Vehicle 2 = 0.9% PEG 3350 ... mannitol

1) System essentially same as [redacted] experiment, except 500mL saline in beaker
2) Vehicle 2 (VF) was used
3) Yonger Wu did the entire study
4) After injection of sample, sample was stirred, flow rate was then increased to 500-800mL/min until echogenic material detected by the oscilloscope, Flow rate then dropped to 100-200 mL/min.
5) The "later window" moved dramatically with each pulse
6) Tubing was manipulated to remove bubbles. At least once (prior to injection 4) this resulted in change of alignment. At that one detected time, the machine was realigned.
7) Cleaning procedure: (1) Water pumped to remove all material, then saline pumped in (2) beaker emptied, saline added + pumped through.

(2) System pumped dry, saline pumped in

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Work [illegible]

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Confidential

4[illegible]-37

Injection #	Sample ID/Mass (Vehicle, mL)	Suspension Preparation	Echogenicity Initial	Echogenicity Over Time	[illegible]
1	Albunex 0.5	NA ([illegible])	[illegible] almost [illegible]		NO
2	Albunex 0.5 mL	NA ([illegible])	[illegible]		NO
3	Albunex 0.3	"	echogenic		[illegible]
4	[illegible] (P)	188 / V [illegible]	not echogenic		NO
5	3-VF-12 mL	V/S2/V [illegible]	a little echogenic	too little to [illegible]	yes
6	4-VF-12 mL	V/S1/V/S1/V [illegible]	slightly echogenic [illegible]	[illegible] over long	yes
7	5-VF-12 mL	V/S1/V [illegible] 10 mL	echogenic ([illegible])	~5-6 min	yes
8	91/080-9 ([illegible]) Sh	1 mL	echogenic <5 ([illegible])	< 1 min	yes
9	94/080-11 ([illegible]) Sh	1 mL	a little [illegible]	< 1 min	NO
10	Albunex 0.5 mL	NA ([illegible])	slightly echogenic [illegible]	[illegible]	yes
11	91/080-5 ([illegible])	V/S1/V/S1/V [illegible]	Lost - bubbles in [illegible]	not longer	[illegible]
12	18-VF-12	V/S1/V [illegible]	slightly echogenic	1-2 min	yes
13	19-VF-12	V/S1/V/S1/V [illegible]	none		yes
14	13-2 mL H2O	Sh 2 mL	[illegible]	1-2 min	yes
15	15-2 mL H2O	Sh 2 mL	echogenic ~ [illegible]	1-2 min	yes
16	8 ([illegible]) Sh	1 mL	echogenic [illegible]	1-2 min	yes

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Injection #	Sample ID/Mass	Suspension Preparation	Echogenicity Initial	Echogenicity Over Time	
	.55				
17	5 ([illegible])	[illegible] 1 mL V/S1/V/S1/V	slightly echogenic [illegible]	[illegible] 1-2 min	yes
18	6-VF-12	a few [illegible] V/S1/V/S1/V	none		[illegible]
19	20-VF-12	a few [illegible] V/S1/V/S1/V 10	none		NO
20	16-VF-12	a few [illegible] V/S1/V/S1/V	slightly echogenic [illegible]	< 1 min	yes
21	11 2 mL H2O	Sh 1 mL	very very slight	< 1 min	NO
22	12-2 mL [illegible]	Sh 1 mL	very very slight	< 300	[illegible]
23	21-VF-12	V/S1/V/S1/V 10 mL	very very slight	< 300	[illegible]
24	14 2 mL H2O	Sh 2 mL	none		NO
25	17-VF-12 mL	V/S2/V 10 mL	none.		NO
26	Albunex 0.5	NA	little echogenic		
27					
28					
29					
30					
31					
32					

Stanley Rue [illegible]
TU
on [redacted]

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2[illegible]
[illegible]-01
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